

SEQUENCE LISTING

<110> Salonen, Jukka T.
 Marchesani, Marja
 Tuomainen, Tomi-Pekka
 Kaikkonen, Jari

<120> A DNA molecule encoding a variant paraoxonase, and uses thereof

<130> Ile102Val, also called Ile101Val variant

<140>

<141>

<160> 4

<170> PatentIn Ver. 2.1

<210> 1

<211> 1068

<212> DNA

<213> Homo Sapiens

<220>

<221> CDS

<222> (1)..(1068)

<223> Coding sequence for variant human paraoxonase (PON1) protein

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atg	gcg	aag	ctg	att	gcg	ctc	acc	ctc	ttg	ggg	atg	gga	ctg	gca	ctc	48
Met	Ala	Lys	Leu	Ile	Ala	Leu	Thr	Leu	Leu	Gly	Met	Gly	Leu	Ala	Leu	
1	5				10						15					
ttc	agg	aac	cac	cag	tct	tct	tac	caa	aca	cga	ctt	aat	gct	ctc	cga	96
Phe	Arg	Asn	His	Gln	Ser	Ser	Tyr	Gln	Thr	Arg	Leu	Asn	Ala	Leu	Arg	
20	25				30											
gag	gta	caa	ccc	gta	gaa	ctt	cct	aac	tgt	aat	tta	gtt	aaa	gga	atc	144
Glu	Val	Gln	Pro	Val	Glu	Leu	Pro	Asn	Cys	Asn	Leu	Val	Lys	Gly	Ile	
35	40				45											
gaa	act	ggc	tct	gaa	gac	atg	gag	ata	ctg	cct	aat	gga	ctg	gct	ttc	192
Glu	Thr	Gly	Ser	Glu	Asp	Met	Glu	Ile	Leu	Pro	Asn	Gly	Leu	Ala	Phe	
50	55			60												
att	agc	tct	gga	tta	aag	tat	cct	gga	ata	aag	agc	ttc	aac	ccc	aac	240
Ile	Ser	Ser	Gly	Leu	Lys	Tyr	Pro	Gly	Ile	Lys	Ser	Phe	Asn	Pro	Asn	
65				70						75			80			

agt cct gga aaa ata ctt ctg atg gac ctg aat gaa gaa gat cca aca	288
Ser Pro Gly Lys Ile Leu Leu Met Asp Leu Asn Glu Glu Asp Pro Thr	
85 90 95	
gtg ttg gaa ttg ggg gtc act gga agt aaa ttt gat gta tct tca ttt	336
Val Leu Glu Leu Gly Val Thr Gly Ser Lys Phe Asp Val Ser Ser Phe	
100 105 110	
aac cct cat ggg att agc aca ttc aca gat gaa gat aat gcc atg tac	384
Asn Pro His Gly Ile Ser Thr Phe Thr Asp Glu Asp Asn Ala Met Tyr	
115 120 125	
ctc ctg gtg aac cat cca gat gcc aag tcc aca gtg gag ttg ttt	432
Leu Leu Val Val Asn His Pro Asp Ala Lys Ser Thr Val Glu Leu Phe	
130 135 140	
aaa ttt caa gaa gaa gaa aaa tcg ctt ttg cat cta aaa acc atc aga	480
Lys Phe Gln Glu Glu Lys Ser Leu Leu His Leu Lys Thr Ile Arg	
145 150 155 160	
cat aaa ctt ctg cct aat ttg aat gat att gtt gct gtg gga cct gag	528
His Lys Leu Leu Phe Asn Leu Asn Asp Ile Val Ala Val Gly Phe Glu	
165 ^{Pro} 170 175	
cac ttt tat ggc aca aat gat cac tat ttt ctt gac ccc tac tta caa	576
His Phe Tyr Gly Thr Asn Asp His Tyr Phe Leu Asp Phe Tyr Leu Gln	
180 185 190	
tcc tgg gag atg tat ttg ggt tta gcg tgg tcg tat gtt gtc tac tat	624
Ser Trp Glu Met Tyr Leu Gly Leu Ala Trp Ser Tyr Val Val Tyr Tyr	
195 200 205	
agt cca agt gaa gtt cga gtg gtg gca gaa gga ttt gat ttt gct aat	672
Ser Pro Ser Glu Val Arg Val Ala Glu Gly Phe Asp Phe Ala Asn	
210 215 220	
gga atc aac att tca ccc gat ggc aag tat gtc tat ata gct gag ttg	720
Gly Ile Asn Ile Ser Pro Asp Gly Lys Tyr Val Tyr Ile Ala Glu Leu	
225 230 235 240	
ctg gct cat aag att cat gtg tat gaa aag cat gct aat tgg ^{act} tta	768
Leu Ala His Lys Ile His Val Tyr Glu Lys His Ala Asn Trp Tyr Leu	
245 250 255 ^{thr}	
act cca ttg aag tcc ctt gac ttt aat acc ctc gtg gat aac ata tct	816
Tyr Phe Leu Lys Ser Leu Asp Phe Asn Tyr Leu Val Asp Asn Ile Ser	
260 265 ^{thr} 270	
gtg gat cct gag aca gga gac ctt tgg gtt gga tgc cat ccc aat ggc	864
Val Asp Pro Glu Tyr Gly Asp Leu Trp Val Gly Cys His Pro Asn Gly	
275 ^{thr} 280 285	
atg aaa atc ttc ttc tat gac tca gag aat cct cct gca tca gag gtg	912
Met Lys Ile Phe Phe Tyr Asp Ser Glu Asn Pro Pro Ala Ser Glu Val	
290 295 300	
ctt cga atc cag aac att cta aca gaa gaa cct aaa gtg aca cag gtt	960
Leu Arg Ile Gln Asn Ile Leu Thr Glu Glu Pro Lys Val Thr Gln Val	
305 310 315 320	
tat gca gaa aat ggc aca gtg ttg caa ggc agt aca gtt gcc tct gtg	1008

Tyr Ala Glu Asn Gly Thr Val Leu Gln Gly Ser Tyr Val Ala Ser Val
 325 330 335 1056
 tac aaa ggg aaa ctg ctg att ggc aca gtg ttt cac aaa gct ctt tac
 Tyr Lys Gly Lys Leu Leu Ile Gly Tyr Val Phe His Lys Ala Leu Tyr
 340 345 350 1068
 tgt gag ctc taa
 Cys Glu Leu stop
 355

<210> 2
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 <212> PRT
 <213> Homo Sapiens

<400> 2

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 Phe Arg Asn His Gln Ser Ser Tyr Gln Thr Arg Leu Asn Ala Leu Arg
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 Glu Val Gln Pro Val Glu Leu Pro Asn Cys Asn Leu Val Lys Gly Ile
 35 40 45
 Glu Thr Gly Ser Glu Asp Met Glu Ile Leu Pro Asn Gly Leu Ala Phe
 50 55 60
 Ile Ser Ser Gly Leu Lys Tyr Pro Gly Ile Lys Ser Phe Asn Pro Asn
 65 70 75 80
 Ser Pro Gly Lys Ile Leu Leu Met Asp Leu Asn Glu Glu Asp Pro Thr
 85 90 95
 Val Leu Glu Leu Gly Val Thr Gly Ser Lys Phe Asp Val Ser Ser Phe
 100 105 110
 Asn Pro His Gly Ile Ser Thr Phe Thr Asp Glu Asp Asn Ala Met Tyr
 115 120 125
 Leu Leu Val Val Asn His Pro Asp Ala Lys Ser Thr Val Glu Leu Phe
 130 135 140
 Lys Phe Gln Glu Glu Glu Lys Ser Leu Leu His Leu Lys Thr Ile Arg
 145 150 155 160
 His Lys Leu Leu Phe Asn Leu Asn Asp Ile Val Ala Val Gly Phe Glu
 165 170 175
 His Phe Tyr Gly Thr Asn Asp His Tyr Phe Leu Asp Phe Tyr Leu Gln
 180 185 190
 Ser Trp Glu Met Tyr Leu Gly Leu Ala Trp Ser Tyr Val Val Tyr Tyr
 195 200 205
 Ser Pro Ser Glu Val Arg Val Val Ala Glu Gly Phe Asp Phe Ala Asn
 210 215 220
 Gly Ile Asn Ile Ser Pro Asp Gly Lys Tyr Val Tyr Ile Ala Glu Leu

225	230	235	240	
Leu Ala His Lys Ile His Val Tyr Glu Lys His Ala Asn Trp		Tyr	Leu	
	245	250	255	
<u>Tyr Phe</u> Leu Lys Ser Leu Asp Phe Asn Tyr Leu Val Asp Asn Ile Ser				
<u>Thr Pro</u>	260	265	270	
Val Asp Pro Glu Tyr Gly Asp Leu Trp Val Gly Cys His Pro Asn Gly				
	275	280	285	
Met Lys Ile Phe Phe Tyr Asp Ser Glu Asn Pro Pro Ala Ser Glu Val				
	290	295	300	
Leu Arg Ile Gln Asn Ile Leu Thr Glu Glu Pro Lys Val Thr Gln Val				
	305	310	315	320
Tyr Ala Glu Asn Gly Thr Val Leu Gln Gly Ser Tyr Val Ala Ser Val				
	325	330	335	
Tyr Lys Gly Lys Leu Leu Ile Gly Tyr Val Phe His Lys Ala Leu Tyr				
	340	345	350	
Cys Glu Leu stop				

<210> 3
<211> 1068
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)..(1068)
<223> Coding sequence for Human Paraoxonase (PON1) gene

<400> 3

atg	gcg	aag	ctg	att	gcg	ctc	acc	ctc	ttg	ggg	atg	gga	ctg	gca	ctc	48
Met	Ala	Lys	Leu	Ile	Ala	Leu	Thr	Leu	Leu	Gly	Met	Gly	Leu	Ala	Leu	
1				5					10					15		
ttc	agg	aac	cac	cag	tct	tct	tac	caa	aca	cga	ctt	aat	gct	ctc	cga	96
Phe	Arg	Asn	His	Gln	Ser	Ser	Tyr	Gln	Thr	Arg	Leu	Asn	Ala	Leu	Arg	
				20					25					30		
gag	gta	caa	ccc	gta	gaa	ctt	cct	aac	tgt	aat	tta	gtt	aaa	gga	atc	144
Glu	Val	Gln	Pro	Val	Glu	Leu	Pro	Asn	Cys	Asn	Leu	Val	Lys	Gly	Ile	
				35					40					45		
gaa	act	ggc	tct	gaa	gac	atg	gag	ata	ctg	cct	aat	gga	ctg	gct	ttc	192
Glu	Thr	Gly	Ser	Glu	Asp	Met	Glu	Ile	Leu	Pro	Asn	Gly	Leu	Ala	Phe	
				50					55					60		
att	agc	tct	gga	tta	aag	tat	cct	gga	ata	aag	agc	ttc	aac	ccc	aac	240
Ile	Ser	Ser	Gly	Leu	Lys	Tyr	Pro	Gly	Ile	Lys	Ser	Phe	Asn	Pro	Asn	
				65					70					75		80
agt	cct	gga	aaa	ata	ctt	ctg	atg	gac	ctg	aat	gaa	gaa	gat	cca	aca	288
Ser	Pro	Gly	Lys	Ile	Leu	Leu	Met	Asp	Leu	Asn	Glu	Glu	Asp	Pro	Thr	
				85					90					95		

gtg ttg gaa ttg ggg atc act gga agt aaa ttt gat gta tct tca ttt	336
Val Leu Glu Leu Gly Ile Thr Gly Ser Lys Phe Asp Val Ser Ser Phe	
100 105 110	
aac cct cat ggg att agc aca ttc aca gat gaa gat aat gcc atg tac	384
Asn Pro His Gly Ile Ser Thr Phe Thr Asp Glu Asp Asn Ala Met Tyr	
115 120 125	
ctc ctg gtg aac cat cca gat gcc aag tcc aca gtg gag ttg ttt	432
Leu Leu Val Val Asn His Pro Asp Ala Lys Ser Thr Val Glu Leu Phe	
130 135 140	
aaa ttt caa gaa gaa aaa tcg ctt ttg cat cta aaa acc atc aga	480
Lys Phe Gin Glu Glu Lys Ser Leu Leu His Leu Lys Thr Ile Arg	
145 150 155 160	
cat ^{aaa} ^{ctt} ^{ctg} ^{cct} aat ttg aat gat att gtt gct gtg gga cct gag	528
His Lys Leu Leu Phe Asn Leu Asn Asp Ile Val Ala Val Gly Phe Glu	
165 ^{Pro} 170 175 ^{Pro}	
cac ttt tat ggc aca aat gat cac tat ttt ctt gac ccc tac tta caa	576
His Phe Tyr Gly Thr Asn Asp His Tyr Phe Leu Asp Phe Tyr Leu Gln	
180 185 ^{Pro} 190	
tcc tgg gag atg tat ttg ggt tta gcg tgg tcg tat gtt gtc tac tat	624
Ser Trp Glu Met Tyr Leu Gly Leu Ala Trp Ser Tyr Val Val Tyr Tyr	
195 200 205	
agt cca agt gaa gtt cga gtg gtg gca gaa gga ttt gat ttt gct aat	672
Ser Pro Ser Glu Val Arg Val Ala Glu Gly Phe Asp Phe Ala Asn	
210 215 220	
gga atc aac att tca ccc gat ggc aag tat gtc tat ata gct gag ttg	720
Gly Ile Asn Ile Ser Pro Asp Gly Lys Tyr Val Tyr Ile Ala Glu Leu	
225 230 235 240	
ctg gct cat aag att cat gtg tat gaa aag cat gct aat tgg act tta	768
Leu Ala His Lys Ile His Val Tyr Glu Lys His Ala Asn Trp Tyr Leu	
245 250 255 ^{Thr}	
act cca ttg aag tcc ctt gac ttt aat acc ctc gtg gat aac ata tct	816
Tyr Phe Leu Lys Ser Leu Asp Phe Asn Tyr Leu Val Asp Asn Ile Ser	
260 265 ^{Thr} 270	
gtg gat cct gag aca gga gac ctt tgg gtt gga tgc cat ccc aat ggc	864
Val Asp Pro Glu Tyr Gly Asp Leu Trp Val Gly Cys His Pro Asn Gly	
275 ^{Thr} 280 285	
atg aaa atc ttc ttc tat gac tca gag aat cct cct gca tca gag gtg	912
Met Lys Ile Phe Phe Tyr Asp Ser Glu Asn Pro Pro Ala Ser Glu Val	
290 295 300	
ctt cga atc cag aac att cta aca gaa gca cct aaa gtg aca cag gtt	960
Leu Arg Ile Gln Asn Ile Leu Thr Glu Glu Pro Lys Val Thr Gln Val	
305 310 315 320	
tat gca gaa aat ggc aca gtg ttg caa ggc agt aca gtt gcc tct gtg	1008
Tyr Ala Glu Asn Gly Thr Val Leu Gln Gly Ser Tyr Val Ala Ser Val	
325 330 ^{Thr} 335	
tac aaa ggg aaa ctg ctg att ggc aca gtg ttt cac aaa gct ctt tac	1056

Tyr Lys Gly Lys Leu Leu Ile Gly Tyr Val Phe His Lys Ala Leu Tyr
 340 345^{Thr} 350

1068

tgt gag ctc taa
 Cys Glu Leu stop
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<210> 4
 <211> 355
 <212> PRT
 <213> Homo Sapiens

<400> 4

Met Ala Lys Leu Ile Ala Leu Thr Leu Leu Gly Met Gly Leu Ala Leu
 1 5 10 15

Phe Arg Asn His Gln Ser Ser Tyr Gln Thr Arg Leu Asn Ala Leu Arg
 20 25 30

Glu Val Gln Pro Val Glu Leu Pro Asn Cys Asn Leu Val Lys Gly Ile
 35 40 45

Glu Thr Gly Ser Glu Asp Met Glu Ile Leu Pro Asn Gly Leu Ala Phe
 50 55 60

Ile Ser Ser Gly Leu Lys Tyr Pro Gly Ile Lys Ser Phe Asn Pro Asn
 65 70 75 80

Ser Pro Gly Lys Ile Leu Leu Met Asp Leu Asn Glu Glu Asp Pro Thr
 85 90 95

Val Leu Glu Leu Gly Ile Thr Gly Ser Lys Phe Asp Val Ser Ser Phe
 100 105 110

Asn Pro His Gly Ile Ser Thr Phe Thr Asp Glu Asp Asn Ala Met Tyr
 115 120 125

Leu Leu Val Val Asn His Pro Asp Ala Lys Ser Thr Val Glu Leu Phe
 130 135 140

Lys Phe Gln Glu Glu Lys Ser Leu Leu His Leu Lys Thr Ile Arg
 145 150 155 160

His Lys Leu Leu Phe Asn Leu Asn Asp Ile Val Ala Val Gly Phe^{Pro} Glu
 165^{Pro} 170 175^{Pro}

His Phe Tyr Gly Thr Asn Asp His Tyr Phe Leu Asp Phe Tyr Leu Gln
 180 185 190

Ser Trp Glu Met Tyr Leu Gly Leu Ala Trp Ser Tyr Val Val Tyr Tyr
 195 200 205

Ser Pro Ser Glu Val Arg Val Val Ala Glu Gly Phe Asp Phe Ala Asn
 210 215 220

Gly Ile Asn Ile Ser Pro Asp Gly Lys Tyr Val Tyr Ile Ala Glu Leu
 225 230 235 240

Leu Ala His Lys Ile His Val Tyr Glu Lys His Ala Asn Trp Tyr^{Pro} Leu
 245 250 255^{Pro}

Tyr Phe Leu Lys Ser Leu Asp Phe Asn Tyr Leu Val Asp Asn Ile Ser
 260 265 270

Val Asp Pro Glu Tyr Gly Asp Leu Trp Val Gly Cys His Pro Asn Gly
 275

275	280	285
Met Lys Ile Phe Phe Tyr Asp Ser Glu Asn Pro Pro Ala Ser Glu Val		
290	295	300
Leu Arg Ile Gln Asn Ile Leu Thr Glu Glu Pro Lys Val Thr Gln Val		
305	310	315
Tyr Ala Glu Asn Gly Thr Val Leu Gln Gly Ser Tyr Val Ala Ser Val		
325	330	335
Tyr Lys Gly Lys Leu Leu Ile Gly Tyr Val Phe His Lys Ala Leu Tyr		
340	345	350
Cys Glu Leu stop		

<210> 5

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer pair

<400> 5

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<211> 21

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: PCR primer pair

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<210> 7

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer pair

<400> 7

ggagaacttttgtggacctg

<210> 8
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer pair

<400> 8
aagtgggcatgggtatacag

<210> 9
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer pair

<400> 9
ctcctccatggttataaggg

<210> 10
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer pair

<400> 10
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<210> 11
<211> 20
<212> DNA
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<220>
<223> Description of Artificial Sequence: PCR primer pair

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<212> DNA
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<220>
<223> Description of Artificial Sequence: PCR primer pair

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<210> 13
<211> 20
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<223> Description of Artificial Sequence: PCR primer pair

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<223> Description of Artificial Sequence: PCR primer pair

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<212> DNA
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<223> Description of Artificial Sequence: PCR primer pair

<400> 16
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<223> Description of Artificial Sequence: PCR primer pair

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<223> Description of Artificial Sequence: PCR primer pair

<400> 18
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<210> 19
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<212> DNA
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<223> Description of Artificial Sequence: PCR primer pair

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gtcttagatactctccacctc

<210> 21
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer pair

<400> 20
ctgaacaagacatggcaaggc